MINUTES OF 338TH MEETING OF REGISTRATION BOARD
HELD ON 04th JULY, 2024

DRUG REGULATORY AUTHORITY OF PAKISTAN
PRIME MINISTER'S NATIONAL HEALTH COMPLEX.
PARK ROAD, CHAK SHEHZAD
ISLAMABAD.

338th meeting of Registration Board was held on 4th July, 2024 in theCommittee Room, Drug Regulatory Authority of Pakistan, Prime Minister's National Health Complex, Park Road, Islamabad.

The meeting was chaired by Dr. Muhammad Fakhruddin Aamir, Chairman, Registration Board, DRAP. The meeting started with recitation of the Holy Verses.

Following members attended the meeting:

1.	Mr. Ajmal Sohail Asif, Director, Division of QA&LT, DRAP, Islamabad	Member
2.	Ms. Aisha Irfan, Director, Division of MD&MC, DRAP, Islamabad	Member
3.	Dr. Ali Jan, Director, DTL, Baluchistan (Online)	Member
4.	Mr. Muhammad Aslam, Additional Draftsman, M/o Law &Justice, Islamabad.	Member
5.	Mr. Ghulam Mujtaba, Deputy Director, Rep. of IPO, Islamabad.	Member
6.	Ch. Zeeshan Nazir Bajar, Additional Director	Secretary
7.	Dr. Naeemulllah Khan, RO, Rep. of M/o NFSR, Islamabad	Member
8.	Mr. Iftikhar A. Chaudhary, Ex-Hospital Pharmacist, Lahore (Online)	Co-optedMember
9.	Dr. Qurban Ali, Ex-Director General, NVL, Veterinary Expert	Co-optedMember

Mr. Nadeem Alamgir, Pharma Bureau(Online) and Mr. Jalal-ud-Din Zafar, PPMA (Online) attended the meeting as observers.

Agenda Item No. I. Division of Pharmaceutical Evaluation & Registration

Registration-II

M/s. Venus Pharma 23 Km Multan Road Lahore.

Assistant Registrar (Writ-I), Lahore High Court, Lahore vide letter dated 15-06-2024 has enclosed order sheet of Lahore High Court, Lahore in W.P No. 37766/2024 dated 13.06.2024 filed by M/s. Venus Pharma 23 Km Multan Road Lahore Vs Federation of Pakistan & others. The Honorable court has ordered as under:

"It is contended by learned counsel that petitioner's application for renewal of registration is pending before respondent No. 03, but the same is not being taken up for decision and in the meanwhile, respondent-Deptt has started taking conceive measures against petitioner. Further submits that he would be satisfied if a direction is issued to respondent No.03 to decide pending application strictly in accordance with law and keeping in view order issued on 01-02-2023, by the Drugs Appellate Board in its 163rd Sitting Held on 20th December, 2022.

2. When confronted, learned Law Officer has expressed no objection on disposal of this petition as requested by learned counsel for petitioner.

3. In view of above, I am inclined to dispose of this petition while directing respondent No.03 to decide pending application strictly in accordance with law and keeping in view above referred order dated 01-02-2023, after hearing petitioner and all concerned, through speaking order within a period of fifteen days from the date of receipt of certified copy of this order.".

Registration Board in its various meetings has considered the case *Registration Status of Formulations (Diclofenac Potassium 75mg & 100mg and Famotidine 10mg/5ml) not approved by Reference Regulatory Authorities & Previous Decisions Taken by the Registration Board in its 250th & 258th* and finally in its 317th meeting held on 16-17 May, 2022 decided as under:

Decision of 317th meeting:

In light of the foregoing discussions, risk-benefit analysis and public health impact of Diclofenac Potassium 75mg and 100mg, the Board made following decisions:

i. Suspended all drug registrations of Diclofenac Potassium 75mg and 100mg under Section 7 (11) (d) read with Section 42 of the Drugs Act, 1976 in the larger public interest, with immediate effect as these are neither approved by any Reference Regulatory Authority nor any safety and efficacy data regarding them is available with any registration holder. Period of suspension will be for one (01) year or till demonstration of its safety and efficacy by conducting indigenous clinical trials in accordance with the Bio Study Rules, 2017 or its approval by the Reference Regulatory Authorities, whichever is earlier. After provision of aforementioned data, cases of such pharmaceutical firms shall be considered on merit by Registration Board.

ii. Suspended manufacturing and import of these drug products immediately and directed to withdraw available stocks from the market in the larger public interest. QA&LT Division, DRAP will monitor and implement the decision in coordination with the respective provincial governments.

iii. Recommended Licensing Division, DRAP for approval of Qualified person for Pharmacovigilance (QPPV) / Local Safety Officer (LSO) whichever is applicable in licensed pharmaceutical units and advised PE&R and BE&R Divisions for implementing similar action for importers of finished drug products as required under Pharmacovigilance Rules, 2022.

iv. Final decision regarding pharmaceutical firms who have obtained interim relief from the Hon'ble Lahore High Court, Lahore shall be announced after decision and direction

by the Hon'ble Court. Legal Affairs Division is requested to place the instant decision before the Hon'ble Court and seek expeditious disposal of the matter in the larger public interest.

v. Recommended DRAP Authority for out of queue consideration of registration applications of Diclofenac Potassium 50mg, 25mg and 12.5mg Tablet and 50mg Sachet in order to facilitate the registration holders affected by the instant decision.

As per above decision of the Board, suspension letters were issued to all manufacturers including M/s. Venus Pharma 23 Km Multan Road Lahore regarding Valron-P 75 Tablets Diclofenac Potassium, Reg. No. 078831 dated 01-06-2022.

Later on various firms have submitted appeals in The Appellate Board against above sated decision of the Registration Board. Accordingly, Appellate Board in its 162nd meeting held on 30th August, 2022 and 163rd meeting held on 01st February, 2023 decided as under:

i. **Allow the appeals and resumption of the manufacturing and sale of the drugs Diclofenac Potassium 75mg & 100mg.**
ii. **The pack size of 100 mg tablet will be reduced to pack of three tablets in order to avoid misuse potential.**
iii. **Sale of both drugs will be prescription only by a qualified practitioner.**
iv. **Pharmacovigilance data will be generated and submitted regularly to the Pharmacy Services Division in accordance with Pharmacovigilance Rules, 2022.**
v. **The manufacturer will provide safety and efficacy studies approved by any credible sources to Pharmacy Services Division for review and submission to Registration Board. If no such studies are available, the PPMA will contact Pharmacy Services Division for conduction of safety and efficacy trial as per Bio Study Rules, 2017.**
vi. **This decision will be applicable to only those firms/companies who are in appeals before the Appellate Board.**
vii. **After the safety and efficacy data establishment, the Registration Board will consider the pending and new applications of this drug.**

Case is submitted before the board for its consideration, in the light of orders of Lahore High Court, Lahore in W.P No. 37766/2024 dated 13.06.2024, please.

Decision of 337th Meeting of Registration Board:

Registration Board, in light of orders of Lahore High Court, Lahore, decided to call M/s. Venus Pharma 23 Km Multan Road Lahore for personal hearing on 04th July, 2024.

Accordingly, firm has been called for personal hearing.

Proceeding of 338th Meeting:

Mr. Sheikh M. Nawaz (Legal Adviser) and Mr. Adnan Tahir (Techinal Person, Plant Head) appeared and submitted authority letter before Registration Board on Behalf of M/s. Venus Pharma 23 Km Multan Road Lahore and presented the case. Furthermore, firm has also submitted the following written statement:

i. We deserve the resumption of manufacturing and sale of drug Diclofenac Potassium 75mg.
ii. We agreed to sale the drug Diclofenac Potassium 75mg tablets by prescription by a qualified practitioner.
iii. Pharmacovigilance data will be generated and submitted regularly to the pharmacy service division in accordance with Pharmacovigilance rule 2022.
iv. We are also bound along with other manufacturers of Para (V) of the Drug Appellate Board's Decision dated 01-02-2023.
v. Being appeals were against General Decision of Registration Board shall apply generally in favor of M/s Venus Pharma also it is respectfully submitted that we are

always obedient to the Decisions/Orders/directions of this respected board strictly in accordance with law.

Decision of 338th Meeting:

After hearing the arguments and perusal of written statement given by the petitioner as mentioned above, Registration Board in light of directions of the Honorable Lahore High Court Lahore vide order dated 13.06.2024 in Writ Petition No. 37766/2024 deliberated that the decision of the Appellate Board dated 01-02-2023 does not bear general/ universal applicability (as para vi of decision recorded above). The aforesaid decision shall be applicable only to those firms/companies who have filed appeals before the Appellate Board. Hence, Registration Board directed to M/s. Venus Pharma 23 Km Multan Road Lahore to submit an appeal before the Appellate Board within 60 days after approval of the said minutes of meeting. Furthermore, fate of the pending application of renewal shall be decided after decision of the Appellate Board.

Agenda Item No. II. Implementation of Bio-availability/Bioequivalence (BA/BE) studies

The Drug Regulatory Authority of Pakistan (DRAP) ensures that all pharmaceutical products conform to acceptable standards of safety, efficacy and quality. All pharmaceutical products, including multisource products, can be marketed only after registration by the DRAP while Multisource pharmaceutical products need to conform to the same appropriate standards of quality, efficacy and safety as required by the originator's (reference) product ensuring that the multisource product is therapeutically equivalent and interchangeable with the comparator product. The implementation of BA/BE studies is the requirement of the law and the International organizations as described under;

- The Section **7 (c) (ix)** of the DRAP Act, 2012 states as under:
  "The powers and functions of the Authority shall be to,- issue guidelines and monitor the enforcement of,- implementation of internationally recognized standards such as good laboratory practices, current good manufacturing practices, good distribution practices, cold chain management, bioequivalence studies, stability studies, anti-spurious codes, clinical trials, biosimilar evaluations, and ***endorsement and systematic implementation of World Health Organization, International Conference on Harmonization and Food and Drug Administration guidelines etc."***
- The Section 3.2.R.3 & 5.3.1 of Form 5F (CTD) under rule 26 (1) of the Drugs (Licensing, Registering and Advertising) Rules, 1976, mandates Bioequivalence Study Reports, submission against which is currently optional vide "Guidance Document for submission of Application on Form 5-F (CTD) for Registration of Pharmaceutical Drug products for Human Use" (PE&R/GL/AF/004), approved by Registration Board. The ICH CTD document also requires the submission of comparative in vivo studies (e.g., bioequivalence) & Comparative BA and Bioequivalence (BE) Study Reports, where applicable.
- WHO Technical Report Series, No. 986, 2014, Annex 6 (Guidelines on submission of documentation for a multisource (generic) finished pharmaceutical product: quality part) requires submission of results from comparative in vitro studies (e.g. dissolution) or comparative in vivo studies (e.g. bioequivalence), when appropriate. WHO GBT sub indicator "MA01.03" mandates the legal provisions that require demonstration of the product quality,

safety and efficacy prior to the registration and/or marketing authorization which includes BA/BE Studies.

2. In pursuance of the above said legal provisions and for adoption of internationally recognized standards and guidelines for evaluation and registration of Pharmaceutical products, DRAP implemented the Form 5-F (Common Technical Data) for Registration of Human Drugs vide S.R.O 713(I)/2018.

3. The Registration Board has adopted a gradual approach for the implementation of CTD leading to a smooth transition and adoption of new format by pharmaceutical industry and initially had granted various exemptions in regard of data requirement. Now, as the DRAP is pursuing the attainment of level III of "WHO Global Benchmarking Tool (GBT) for Evaluation of National Regulatory System of Medical Products" ***the procedures of regulatory approval related to registration of generic drugs, shall be made in line with the guidelines of international regulatory agencies, for which implementation of Bio-equivalence study should be initiated,*** since it is the mandatory requirement of WHO GBT Level I stage.

4. In this regard DRAP is initiating the implementation of BA/BE studies to comply with the international regulatory standards which is also of prime importance to enhance the exports of Pakistani Pharmaceutical Industry. Keeping in view the above, the optional status of submission of BA/BE studies is hereby withdrawn and now it is mandatory to submit BA/BE studies as per ICH CTD guidelines.

Decision: In the light of S.R.O 713(I)/2018 and requirement for WHO Listed Authorities i.e in particular the Maturity Level-1(ML-1) "the procedures of regulatory approval related to registration of generic drugs, shall be made in line with the guidelines of international regulatory agencies, for which implementation of Bio-equivalence study should be initiated." The Board decided the systematic implementation of Bio-equivalence study in accordance with the WHO and International guidelines.

The Board also suggested to the Division of Pharmacy Services, DRAP to facilitate the process of establishment/approval of new centres for BE studies as per the Bio Study rules 2017.

Meeting ended with vote of thanks to & from the chair.